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(54) Title: MODIFIED DEACETOXYCEPHALOSPORIN C SYNTHASE (DAOCS) AND X-RAY STRUCTURE

(57) Abstract

Three-dimensional crystal structure(s) of deacetoxycephalosporin C synthase (DAOCS) are described. The X-ray co-ordinates provide precise 3-dimensional information of amino acids within the structure of DAOCS. Some of these are in complexes with iron and/or substrates. Information from the structures is used to modify enzymes of the cephalosporin biosynthesis pathway including DAOCS, deacetylcephalosporin C synthase DAOC/DACS, such that they accept unnatural substrates (e.g. penicillins G, V) in order to improve the production of beta-lactam antibiotics. The structures may be used to predict the structures of other 2-oxoglutarate dependent enzymes, thereby allowing the design of inhibitors, and new catalysts for the production of e.g. oxidised amino acids/peptides. Specific modifications of amino acid residues are proposed and exemplified.